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RADIUM

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VOL. IV NOVEMBER, 1914 No. 2

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A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES

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RADIUM

A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY, PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES.

Edited and Published by Charles H. Viol, Ph. D. and William H. Cameron, M. D., with the assistance of collaborators working in the fields of Radiochemistry, Radioactivity and Radiumtherapy.

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VOL. IV NOVEMBER, 1914 No. 2

RECENT AMERICAN CONTRIBUTIONS TO RADIUM THERAPY, II.

Joseph B. *Bissell, M.D.* (New York). The Surgical Status of Radium Treatment of Cancer. International Journal of Surgery. September, 1914, pp. 324-5. In an editorial, Dr. *Bissell* makes the following statements.

"The place which radium is to occupy in surgical therapeutics is now quite well defined. We have derived knowledge enough from the experiences of competent observers and skilled surgeons in the last decade to allow a more thorough preliminary determination of its true value. Foreign medical literature contains many valuable papers on this subject; much has also been published in English. In this country extravagant claims of its therapeutic utility as well as many serious denials of its curative power have been placed on record in the public press as well as in the medical journals. Without doubt this futile discussion has postponed the acquirement of definite knowledge of the action of radium. Capable observers whose scientific knowledge and surgical skill are beyond question, have testified to numberless cures in the malignant types of disease susceptible to its action."

"Reports of failure have undoubtedly often been due to poor technic and faulty diagnosis as well as misapplication of the agent. Often the amount of radium used has been too small for the size of the tumor attacked. Cases are on record where not only an inferior grade of the radium salt has been employed, but even where for all purposes of treatment no radium at all was present in the material used. Only in the past year or two has it been possible to obtain radium of a good quality, of a definite

purity, and in exact measurements; in the earlier days of its employment, malignant growths and various other pathological conditions were treated in what we now know to have been a haphazard and irrational manner. At one time radium was obtained from irresponsible sources, and beyond the fact that some radiation was present nothing was known as to the exact amount or as to its activity or strength or dosage. A case in point was that of a physician in this city who carried with him, in an unprotected glass tube, a quantity of a greyish white powder said to be the mineral in question and which was supposed to have been procured from Madame *Curie* herself in the early days of its discovery. This doctor had reported some cures of cancer by this material, but later he had treated several cases which failed to improve, and as a result of these failures the value of radium in cancer was vigorously denounced by him. He was persuaded to have the powder in his possession measured and examined. This was done in a laboratory, and the tube was found to contain an infinitesimal amount of radium, about twelve dollars worth in all. Comment is unnecessary."

"In the past few years several Radium Institutes as well as private owners of radium have had within their control definite and adequate amounts of this agent and an abundance of clinical material, so that from their experience it is possible to draw fairly satisfactory inferences as to the reliability of some of its surgical applications. There are still "doubting Thomases" of the surgical world who affect to believe that radium is of no value whatever in the treatment of cancer. It is of course needless to say that they probably never had any experience of their own with real radium and never have seen it properly employed. There are still surgeons known to the writer who refuse to admit the favorable results from the intravenous use of salvarsan and neosalvarsan in syphilis. Such men cannot be convinced by either argument or observation. Time alone can teach them. The vast majority of surgeons and medical practitioners are now well satisfied that radium possesses certain fixed and decided therapeutic properties. It is necessary that these should be accurately known. It remains for us still to define the class of malignant cases best treated by radium, the dosage, the amount necessary in a given case, the length of time it is to be applied, the site of the application upon or about the tumor, and the period in the growth of cancer when it is most susceptible to the effect of radium. The best clinical filtration in each case must be determined by proper and scientific methods. * * *.

"Most growths of perceptible size require a considerable amount of radium element to produce a cure. Small epitheliomata of the skin require, as a rule, from 10 milligrams up, depending upon the length of time of the exposure. Disappointment will follow the operator who tries to cure all of the various growths, malignant or otherwise, with less than 100 mgm. of the radium element. This may be true even if he is able to take long periods of time in the application. Undoubtedly cases of cancer have gone to their death from failure to use a large enough amount of radium, or because an impure and weak salt, or because of the

too few milligram hours exposure, or because of too large a tumor in proportion to the amount of radium available."

"Radium is an exceedingly reactive metallic element, difficult to isolate and keep in its pure state. The material which is contained in the tubes in use is a salt of radium, usually a double salt with barium. It is either the sulfate, the bromide, or the chloride, as a rule. The value of the salt is estimated by the quantity of radium element present in each combination."

"Whether radium cures by selective affinity, or by changing the disorderly cells into orderly ones, or whether it stops the growth of neoplasms by blocking the nourishment by a process of endarteritis or whether anti-bodies are produced by the irradiation, or whether it performs its work by a combination of all of these factors, is a question for speculation and argument as well as observation. As compared with the results obtained by operative removal of new growths radium holds a very enviable reputation. As an adjunct and as a supplemental treatment to the knife it is of distinct value. With the knowledge that we now have of its action in cancer, it would appear to be the duty of the surgeon to resort to its use under certain circumstances before and after operation."

"Some of the indications for the surgical use of radium are as follows: In cancer, as an adjunct to the knife before and after operation. On parts of the body inaccessible to the knife; in cases where the tumor cannot be excised without permanent damage or danger to life; where most of the cancer has been cut out, but complete removal is impossible. In various forms of malignant disease which are particularly susceptible to radium application, as for instance rodent ulcer, round cell sarcoma, basal cell epithelioma, and other forms of superficial or skin epithelioma; also in cases where for cosmetic reasons operation is refused. Furthermore, in incurable cancer to relieve various symptoms, such as odor, discharge, pain; and last, but not least, to sustain the patient and improve the general health, in connection with other palliative measures, thus taking away from the sufferer the certainty of death and reviving confidence and hope."

"To obtain its most beneficial effect radium should be employed, for the present at least, only by a well qualified expert who is experienced in its application and who has a wide knowledge of the special technic, the proper filtration, the time of exposure, and the amount necessary in each given case; one who is familiar with the local effect of radiation upon the lesion itself and upon the skin and the surrounding structures as well as with all the other details necessary to a successful result. The expert ought to be a clinician understanding the various pathological conditions in which radium is indicated, as well as a surgeon of capability, skill, and experience."

Isaac *Levin*. (New York). The Relation Between the Surgical Treatment and Radiotherapy of Cancer. Medical Record, October 10th, 1914, pp. 615-20.

With regard to the use of radioactive substances in the treatment of cancer, Dr. *Levin* says:

"The rationale of the radiotherapy in malignant tumors must be looked for in the so-called selective action of the rays on the cancer cell. The Roentgen rays and the rays of the radioactive substances are absorbed by the cells of the radiated tissue. Through the biochemical action of the rays the cells become diseased. The injury caused in the cells by the radiations may differ in degree in accordance with the quantity of the rays absorbed. Cells only slightly injured may recover while a severer injury may completely destroy the cell. Every cell of the animal or plant organism is susceptible to injurious action of the radiations. But the susceptibility varies in degree with the cells of different tissues. The cells of malignant tumors are a great deal more susceptible to the action of the rays than the cells of the normal tissues surrounding the tumor. If the rays are employed of a correct quality and in a sufficient quantity, it is possible to destroy all the cancer cells in a certain locality and at the same time leave the normal tissues either intact or so slightly injured, that they ultimately recover. This quantitatively selective influence of the rays may reach to a depth of at least three and one-half cm.

Technique of Radium Therapy. "The alpha and beta rays which constitute the greater part of the radiation are called soft rays and have little power of penetration. They are absorbed completely by the superficial layers of tissue, and the quantity absorbed by each cell is so great that all the tissues are destroyed, and the action of the rays is caustic. The hard gamma rays represent only about 1 per cent. of the radiation, they penetrate into the deeper layers of tissue and exert the selective action on the cancer cells. It is possible that a small percentage of the hardest beta rays have a similar action. With the small quantities of radium used formerly the gamma rays had no influence on the tissues. The modern method of radium therapy consists in employing larger quantities of radioactive substances and applying them for a longer period of time. The soft caustic alpha and beta rays, which would be very injurious with the larger quantities of radium used, are filtered off by layers of some heavy metal which absorbs the soft rays. The methods vary with the different investigators, some of them employing extremely large quantities of the substance as high as 800 mgm. of mesothorium at one time. Recently it was shown that with such extremely large quantities the selective action may again be lost and the whole organism of the patient injured. It would lead too far to describe all the various methods employed and the writer will present only his own method of application of radioactive substances."

"The radium salt is sealed in thin glass tubes and these placed in a silver tube 0.5 mm. thick. When the surface of the tumor is ulcerated or the radium is placed inside of a tumor, the silver tube is covered only with a thin layer of rubber and then the harder beta rays also come into use. But in the majority of cases only the gamma rays are used, and for this purpose the silver tube is placed inside of a brass tube 0.75 mm. in thickness. The brass tube is further covered with several layers of photographic paper and cotton in order to protect the skin against the irritating

secondary rays which are produced in the metal filters under the influence of the gamma rays of the radium. The whole is placed in an aseptic rubber tube. The largest quantity of radium used on a patient at one time is 50 mgm., which is kept continually over the growth for 2, 4, 6, or 12 hours. When the malignant growth is extensive, as in carcinoma of the uterus, the urinary bladder, or the breast, the writer applies the radium for 12 hours of the night every other night until 100 hours of 50 mgm. or 5,000 milligram-hours have been given; after this a recess is taken for four weeks and then if necessary another shorter course of treatment is given. This method of the writer implies the use of a comparatively smaller quantity than is recommended by some clinicians. But the results are quite as satisfactory, while the severe injuries to the adjacent normal tissues caused by the very large doses are avoided. Very recently there appeared an article by *Schauta,* a noted German gynecologist, in which he states that he has employed radium in carcinoma of the uterus by three different methods. At first he used very small quantities of unfiltered radium and the results were all negative. Then he applied very large quantities of radium for several days in succession, and while the malignant tumors disappeared the patients died as a result of injuries of the normal tissues. At present he employs as a maximum dose 50 mgm. during 12 hours. As a result of this method not a single patient of *Schauta* died, and 50 per cent. of the patients are clinically cured. His technique is practically identical with the one employed by the writer and reported by the latter on a previous occasion."

"The Relative Value of Radium and Roentgen Rays.—When *Becquerel* first discovered the radioactive substances he called his radium tube a pocket edition of the Roentgen tube. This expression very aptly shows their relative position. The biological action of the two kinds of rays is probably very closely analogous, though some investigators claim that there is a qualitative difference in their action on cancer cells. At least cases are on record in which one kind of rays failed and the other kind influenced the growth. The rays of the radioactive substances are a great deal more penetrating than the hardest Roentgen rays which can be produced today and the former can be placed close to the diseased area, while the distance between the anticathode and the skin is not less than about 15 cm. In conditions like carcinoma of the larynx, esophagus, rectum, or vagina, the radioactive substances which can be placed within the lumen of the organ are superior to the Roentgen rays. On the other hand, the Roentgen rays can be used over a larger area and are therefore more advantageous in carcinoma of the breast, or stomach, or in large round-cell sarcomata, lymphosarcomata, mediastinal tumors, etc."

"Rationale of the Combined Surgical Treatment and Radiotherapy in Cancer.—Both surgery and radiotherapy are local methods of treatment, and a general dissemination of the disease or metastases in distant organs is at present beyond their reach in the majority of cases, though *Kroenig* and *Bumm* reported cases of a metastasis in the lung anatomically cured by radiotherapy. Success in cancer therapy depends upon the destruction of all

the cancer tissue in the organism. The advantage of surgery consists in the fact that it removes immediately at one sitting everything diseased. On the other hand it removes with it at the same time a great deal of adjacent healthy tissue. A limit is set to this removal of normal tissue by the fact that vital organs may be injured and consequently the life of the patient endangered. As a result of this a large percentage of cancer patients, as stated above, are inoperable and in a great many of those operated upon there are left microscopic islands of cancer tissue, no matter how radical the operation. These small islands develop subsequently into secondary tumors, and the disease recurs. The main advantage of radiotherapy, on the other hand, consists in the fact that it may destroy such small islands of cancer tissue without injuring the adjacent normal tissue. The disadvantage of radiotherapy consists in the fact that with our present technique it does not reach beyond a certain depth, and while it destroys the upper layers of a large tumor, the lower part may continue to grow."

"The great advantage of the combined treatment is thus self evident. Surgery must remove the gross tumor whenever possible and radiotherapy must destroy the small islands of cancer tissue which cannot be seen by the naked eye of the operator and which are left behind in the greater number of cases notwithstanding the most radical operation. In other words, the treatment of a cancer patient is not complete unless the operation is followed for a certain length of time by radiotherapy. Cases considered to be inoperable, i. e., those in which all of the cancer tissue cannot be removed and a radical operation cannot be performed, should be operated upon with the aim in view to remove the greatest mass of the cancer tissue. This should be followed by radiotherapy in order to destroy the small disseminated remnants of cancer tissue. A number of inoperable cases of carcinoma have been reported recently which were improved under radiotherapy to such a degree that subsequently a radical operation could be performed. These cases, no matter how rare they may be, show the urgent necessity for radiotherapy in all inoperable cases not only as a most potent palliative measure, which removes the fetid obnoxious discharge from cancerous ulcerations and diminishes pain, but also as a preliminary to subsequent surgical treatment. As stated above, at the most only 30 per cent. of all cancer cases remain cured for five years and over after a radical operation. If radiotherapy should change the figure only to 35 per cent. the method of treatment is more than justified. From all the aforesaid it is self-evident that the ideal method of treatment of malignant growth consists at present in the correct combination of surgery and radiotherapy."

"Classification of Malignant Tumors in the Light of Combined Treatment.—To facilitate the consideration of the value of combined treatment in the various forms of malignant tumors, it may be well to divide them into groups as is seen on the chart.

(A) *Carcinoma.*

(1) Superficial: Seated in and under the skin. Ulcus rodens, skin, lip, penis, breast, thyroid, parotid tumor.

(2) Deep: Seated in and under the mucuous membranes. Uterus, rectum, vagina, prostate, esophagus, mouth, tongue and pharynx, larynx, urinary bladder.

(3) Internal: Seated in and under the serous membranes. Ovaries, stomach, intestines, liver, gall-bladder, pancreas, lungs, mediastinum, kidney.

(B) *Sarcoma.*

"The first group of carcinoma is the most easily influenced by the rays. In ulcus rodens and superficial epitheliomata of the skin, radiation undoubtedly accomplishes as much as the knife. It may even have certain advantages, both cosmetic and in the fact that it does not open the lymph and blood channels and thus allow freed cancer cells to enter the circulation. Very favorable results are obtained by radiotherapy in carcinoma of the penis, the breast, the thyroid, and in parotid tumors. But whenever possible, an operation should be performed as a preliminary step to radiation and as much as possible of the primary tumor and of the involved regional lymph-glands should be removed. But the radiotherapy should follow immediately, otherwise the tumor after a partial operation becomes frequently very malignant and cannot be influenced by the rays subsequently."

"Carcinomata of the second group are situated within comparatively easy reach of the rays, do not attain very great size, and present good subjects for radiotherapy. As stated above, tubes of radioactive substances may be placed in close proximity to all the parts of the growth. Indeed the most favorable results are obtained in the treatment of carcinoma of the uterus. In a certain number of cases inoperable conditions with involvement of the broad ligaments have been rendered operable by a preliminary radiation. In some of these cases the extirpated uteri did not show any cancer cells on microscopic examination. The other organs of the same group do not yield quite as good results as the uterus. The writer and other clinicians have seen marked improvement in carcinoma of the vagina, the larynx, the urinary bladder, the rectum, prostate and esophagus. Carcinoma of the mouth, tongue and pharynx usually do not respond well to radiotherapy. Of the latter conditions carcinoma of the tongue is the most refractory. Most probably the cancer cells in these conditions are unusually resistant to the action of the rays. Generally, it must be remarked that cancer cells of the same anatomical structure but originating in different organs or even in the same organs of different individuals may react quite differently to the action of the rays. The work is still in the beginning and improved methods will undoubtedly improve the results. This second group of cases will probably become the true domain of radiotherapy. But for the present in this group of cases radiotherapy should also precede or follow surgical treatment and be employed alone only when the case is completely inoperable. Even then it is advisable to remove the greater part of the tumor with the knife or diathermy and then radiate. Furthermore, the preliminary operations of colostomy, gastrostomy, tracheotomy, etc., are frequently needed in order to facilitate the application of the rays."

"The third group of cases of carcinoma is the least amenable to radiotherapy. Still there are cases on record in which carcinoma of the stomach, the large intestines, and even the lungs have been very favorably influenced by the rays. *Werner* and *Kroenig* report two cases of carcinoma of the stomach which disappeared under radiation. Whenever an exploratory laparotomy is done and an inoperable carcinoma of the viscera is found, the tumor should be brought if possible nearer to the abdominal wall, so that it may be influenced subsequently by the rays."

"Sarcomata are as a general rule influenced by the rays a great deal easier than carcinomata. But here again the best procedure is to remove surgically as much as possible of the tumor, even if the operation cannot be performed radically, and then follow immediately with radiotherapy."

"To recapitulate, the advisability of radiation as an only method of treatment of operable cases of cancer, which is advocated by many noted German gynecologists, must be questioned until a sufficient number of years have passed to show the permanency of the reported cures. On the other hand surgical treatment of malignant tumors is never complete unless it is combined with radiotherapy. All inoperable cases should be radiated, not only as a most excellent palliative measure, but in the hope, small as it may be, that the cases may either become operable or else the disease may be arrested, and the patient may gain months, nay years, of comfortable life. In such inoperable cases when the tumor growth is extensive it may be advantageous to destroy the greater mass of the tumor by the aid of the knife or diathermy and then radiate. In any event the diagnosis of an inoperable malignant tumor should not be the equivalent of a death warrant to the patient."

W. H. B. *Aikins* and K. M. B. *Simon.* (Toronto). The Histological and Clinical Changes Induced by Radium in Carcinoma and Sarcoma. Dominion Medical Monthly, September, 1914, pp. 97-107. (Illustrated with seven photomicrographs).

"The histological changes induced by the action of radium rays have been reported from time to time in medical literature. In order to confirm these for our own satisfaction a study was made of tissue removed from two cases under radium treatment, and careful observation made of the cellular changes."

"The first case was one of adeno-carcinoma of the breast. This patient had been referred for radium treatment nearly two years ago by Dr. G. P. *Sylvester.* He had removed the right breast for carcinoma twelve years before. There had been no evidence of recurrence until the summer of 1912, when a mass appeared in the right axilla. An operation was performed at which as much as possible of this mass was removed. It was impossible to clean the axilla entirely as the growth was adherent to the large vessels. With the object of destroying that portion of the growth which could not be removed, radium exposures were given. When the treatment was begun there was a perceptible thickening of the axillary tissues and some considerable edema of the arm. Under

treatment the parts regained their normal, the mass disappeared and the swelling of the arm subsided. This favorable condition of the right side has persisted, and there is now no evidence of malignancy in that region."

"In March, of this year, the patient spoke of a lump in the left breast, and on examination, a hard mass of induration, about one and a half inches in diameter, about the nipple was found, together with an enlarged axillary gland. There was retraction of the nipple. The patient was advised to have immediate operation, but this she did not wish to undergo at the hands of any other than Dr. *Sylvester,* so as a compromise it was decided to irradiate the parts, with the hope of retarding the progress of the disease until her surgeon's return. This was accordingly done by Dr. F. C. *Harrison,* a careful watch being kept over the condition until the end of May, when the breast was removed. Portions were obtained for examination, and the pathologist's report indicates the effect of the radium rays in the cancer cells."

Pathologist's Report. "A specimen of what proved to be an adeno-carcinoma of the breast was submitted to us after being subjected to the influence of radium. We found the upper portions of the skin which previously had been reported to be infiltrated with the growth to be totally free from any remains of malignant tissue. Deeper in the tissue, however, there seemed to have survived a diffuse growth, the cells smaller as we neared the surface. These cells would also have been destroyed had radiation been continued."

"We noticed that some of the carcinomatous cells were markedly hypertrophied, some were monstrous, some vegetative, whilst the protoplasm showed marked eosinophila, proving beginning degeneration. The various tissue elements had become broken up and eosinophilic, young fibroblasts had evidently replaced the growth in the parts nearer the surface."

"The second case from which we were able to obtain specimens was that of a railway fireman, twenty-eight years of age, referred by Drs. Bruce *Riordan* and R. A. *Thomas.* He received a blow over the right tibia in March, 1913. A swelling persisted and was incised in January, 1914, under the impression that it was an abscess."

"A report of the tissue examined was that it was a myeloid sarcoma, but the development of a secondary mass in the right groin indicated that is was of a more malignant type, and on a second examination the tumor was found to be a round-celled sarcoma. Dr. *Riordan* wished him to have the benefit of radium, although the case was most unfavorale owing to metastatic development."

"Radiation was accordingly undertaken, and three weeks later a portion of tissue was removed for examination from the primary lesion. The striking changes induced by the radium rays are very apparent, and are particularized in the pathologist's report."

Pathological Report of Specimen. "The tissue consists of a portion of a large fungating growth removed from the anterior surface of the thigh."

"The epidermal elements have completely disappeared and their place taken by a large fungating tumor which clinically is sarcomatous. On microscopic examination one sees that this is a large celled sarcoma with very large cells and a few spindle cells. The sarcomatous tissue infiltrates all around it, there is no tissue reaction, but a connective tissue stroma is present which is edematous and filled with a pigment which is evident hemosiderin. The nuclei are often very large and measure about 16 x 15 microns. The size varies, but everywhere it shows mitotic figures and conform to all the characteristics of malignant sarcomata."

"On June 4th the tumor was exposed continuously to the radium rays, a dosage of 240 centigram hours being given, and on June 15th another portion was removed."

"Here we see wonderful changes. In place of the sarcomatous fungating mass we find a mass much reduced in size. The large cells of the growth under the influence of the rays have changed to smaller connective tissue cells and spindle cells. The cells show necrosis and necrobiosis. The connective tissue cells have been mobilized and also the leucocytic infiltration is most intense; due doubtless to the trophic stimulus the connective tissue has become vascularized not by a mere inflammatory reaction, but by a truly specific stimulus, which has expressed itself in the definite form of connective tissue elements."

"From a review of the literature and study of our specimens we are forced to conclude and agree with other original workers that due to the influence of radium the tumor cells undergo necrosis or necrobiosis. The connective tissue cells are mobilized and also leucocytic infiltration supervenes, due to the trophic phenomena stimulated, the connective tissue becomes vascularized in the usual way, not by a mere inflammatory repair, but by a true trophic stimulus which expresses itself in a definite form of connective tissue, with fibres parallel to the surface radiated."

"On close perusal of the current and past literature we find meagre reports. On similar studies, however, *Dominici* and *Barcat* experimentally produced radium burns and which on healing they showed to be composed of fibroblasts and connective tissue bundles parallel to each other and parallel to the surface of the skin. They found that the fixed cells became rarified, the chromoplasm of the parenchymal cell disappeared and becomes changed into hyaloplasm, the connective tissue bundles separating and the fibroblasts thickening."

"Thus they also discovered that those portions of the tissue which had been subjected to radium become essentially differentiated from those not affected, by the alteration and regular direction of the connective tissue bundles."

"Their texture is somewhat analagous to a flat fibroma with connective tissue bundles arranged in regular manner."

"*Degrais* and *Bellot,* in a recent article, pointed out that when epitheliomatous cells are exposed to radium there is a hypertrophy of the nucleus and degeneration of the protoplasm, and a certain amount of keratinization takes place. At later dates, 20 days or so after radiation, these epitheliomatous masses become trans-

formed into keratinized debris. The formed elements break up and disintegrate; young fibroblasts and connective tissue cells, lymphatic cells and polymorphonuclear cells infiltrate the growth and carry on a phagocytic function, and meanwhile cicatrization occurs at the expense of the hyperplastic and regenerated stroma of the tumor."

"In the Freiburg Clinic, *Aschoff, Kroenig* and *Gauss* obtained results similar to these. *Kroenig* and *Gauss* also report the disappearance of myomata by means of radiation of mesothorium. In a recent number of *Progressive Medicine,* a review of the article by *Gauss* shows ten pieces of tissue excised from time to time during the course of treatment; these revealed such striking changes as in some instances to lead to a suspicion of a mixing of the specimens, so wonderful are the changes. For instance, one tissue at the beginning shows an adeno-carcinoma. Two weeks later it shows connective tissue and cancer nests. Three weeks later it shows benign tissue with epithelial debris."

"*Doederlein* has reported several cases where carcinomatous cells have necrosed, and it seems that the connective tissue takes a new life after being relieved of the products of carcinoma cells."

"*Teitschlaender* reports that with mesothorium the cells increase in size, lose their characteristic form and increase in the size of the nuclei. There is pyknosis, round-celled infiltration and eosinophilia. Thus the chief action of mesothorium on carcinoma seems to be the inhibition of karyokinesis and activation of leucocytes and destructive changes, allowing the normal tissue to regenerate."

Conclusions. "In sarcomata the retrogression takes place according to the following law:

"1. The size of the body and of the nucleus of the large cells decreases."

"2. As they shrink the neoplastic elements elongate, the shape of the nucleus becomes regular, and they eventually assume the form of large embryonic connective tissue cells, forming into a celled mass similar to that of a true fibroma. Thus we may emphasize the fact that sarcomata are transformed by radium into a tissue analagous to that of a fibroma with myxomatous changes."

"As regards epitheliomata and carcinomata, under the influence of the radium rays, the following change takes place:

"1. The cells gradually diminish in size and staining properties."

"2. This atrophy corresponds not to the metamorphosis of these definite formed elements, but to their destruction as shown by keratinization or absorption."

"3. The epitheliomatous cells disappear either by means of progressive absorption of protoplasm and nuclei through the leucocytic infiltration or by a sort of granular degeneration."

"The other processes associated with the development of every epithelial tumor are arrested, while vascular connective tissue is organized according to the method just described."

"4. As proof that the changes initiated by radium in the tumors are such as to lead to immunity, great importance must be attached to the cellular infiltration, first leucocytic, then later

a round-celled infiltration. It has been recently shown these require different reactions of the tissues for their function, hence radium must affect the blood. These infiltrations have always been noted in all cases of experimental transplantation of malignant cells, and always accompany the cases in which the animal becomes immune and the tumor disintegrated."

Joseph B. *Bissell,* M. D. (New York). Some Radium Therapeutics. Medical Record, July 11th, 1914, pp. 55-56. The author briefly describes the physical properties of the radium rays, and the effects of the local application of radium in the treatment of various benign and malignant conditions. He says: "In internal medicine no less an authority than von *Noorden* recommends its use in many pathological conditions."

"For the purpose of the injection radium in the form of the bromide is dissolved in saline solution. This is enclosed in a glass ampulle put up aseptically in the laboratory. Each ampulle contains 50 micrograms of the salt, but if desired 25 micrograms or 100 micrograms can be easily put in this glass container."

"In cases where radium is prescribed by mouth the dose is 1 microgram of radium bromide in solution. Each dose is put up in a separate bottle. It is taken three times a day before meals. A special glass or straw tube comes with each bottle. In some cases bath water was also used, and where the joint pain was very severe radium pads were applied. In every patient with arthritis, efforts were made to ascertain the cause of the joint infection and if possible to remove it. Blood pictures were taken before and after treatment. The blood pressure and the coagulation time of the blood were taken before and after each injection. Accurate observation of symptoms and functions were noted before, during, and after treatment, in order if possible to draw definite conclusions as to the value of radium therapy."

Case reports are given on six cases of arthritis in which radium was used internally in the form of radium drinking water and by intravenous injection. In all the cases there was a marked improvement in the patient's condition. In one case of arteriosclerosis and nephritis in which the radium was used by intravenous injection there was a fall in blood pressure from 230 to 160. The case was hopeless when first seen, the man being "water-logged with ascites and suffering from alcoholism."

"Two cases of arteriosclerosis at Bellevue also received one injection each in order to study its effect upon blood pressure. One was a heavy beer drinker with contracted kidney, whose pressure was reduced from 156 to 140 in the first 24 hours. The blood pressure of the other was reduced from 160 to 140 in the same length of time by the injection of 50 micrograms."

"No reaction was noticed following the injections except in one case a severe headache the next day, and in another case slight chill, fever and increase of pain about the joints for two hours. No local reaction was noticed in any of the intravenous injections. Most of the writers on the intravenous use of radium record an increase of pain and swelling about the affected joints, but with the one exception mentioned above it did not occur in my cases."

"In the literature of radium treatment a reaction is considered to be rather a good sign and improves the prognosis."

"From a study of these nine patients the following facts concerning radium therapy may be assumed: Radium injected into the veins relieves pain; it improves the blood picture in anemic and cachectic patients; it causes absorption of deposits around chronically infected joints; it reduces high blood pressure, lessens the coagulation time, and has a certain definite effect as a hypnotic."

C. Augustus *Simpson.* (Washington, D. C.). The Relative Value of Radium and X-Ray in Treatment of Skin Diseases and Cancer. Southern Medical Journal, October, 1914, pp. 818-25. The author apparently has had no personal experience* in the use of radium. The main object of his paper is to show that the X-rays can be used as effectively as radium, where radium has any therapeutic value and further that the X-ray is more effective than radium. He says: "One not acquainted with the facts would be led to believe that the profession was just beginning to understand the action and effects of radium. The principal skin clinics of Europe have for some years been supplied with the substance in suitable form and quantity to treat dermatological diseases. There is no secret in their method of applying it, and any medical man interested in its use has ample opportunities to witness the results they obtain. In Berlin, Vienna and London I saw skin cancers and warts cured and partially cured by radium, but I am confident that any experienced dermatologist could have obtained equally as good results with arsenical and thorium paste or the acid nitrate of mercury. If he were qualified and understood the technique of giving massive doses of X-ray the same or better results could be had by an exposure lasting about one-fifth the time required by radium. Even with the older X-ray technique, which I consider dangerous and a relic of the past, many cures were produced. Some physicians, as *Pusey* and *Pfahler,* became so expert, even without the aid of the pastiles and radiochronometers, that they were able to cure the great majority of these lesions, although requiring a great many exposures to do so. Such experts were by no means common, and America can boast of very few men sufficiently interested in therapeutic work to develop a technique which could bring about such uniformly good results. Inaccurate exposures, burns and relapses caused by the

*One who has not a first-hand knowledge of the value of a therapeutic agent such as radium or the X-rays is hardly in a position to make an estimate of comparative values. As has frequently been pointed out, poor results with the radium and X-rays often are caused by poor technique or inadequate quantities of radium. For this reason it is not wise to accept all poor or negative results unreservedly. It would be useless to deny that radium has produced remarkable results and it is only justice to suffering humanity that this substance should be given a thorough trial where it might promise good results. Time alone can decide the rather difficult question of the relative value of radium and other therapeutic measures in the treatment of any given condition.—Editor.

efforts of men poorly instructed in the use of such a dangerous apparatus placed X-ray therapy in the discredited position it now occupies, and while Europe and England have adapted the new massive dose method with its resulting successes, America seems very slow to forget past injuries."

Referring to the comparative value of radium and X-rays in the treatment of skin diseases the author says "the advantages from all reports are still to be found with the X-ray." After citing conditions in which radium has not been successfully used he says in discussing the use of the X-ray: "Our exact knowledge of the sensitiveness of these individual lesions to X-ray is at the present time most unsatisfactory and will remain so until the X-ray men can come together, compare notes, formulate rules and systematize X-ray treatments. After this it will be possible for the physician to prescribe and administer the desired curative quality of X-ray to his patients as accurately as he prescribes and gives drugs. Those men that insist on giving X-ray without any method of dosage other than guesswork should be made to realize how much they are retarding Roentgen therapy in this country."

And again further on he says: "With the new *Coolidge* tube, probably the most dangerous instrument ever placed in the hands of the profession, extreme care must be exercised to insure correct dosage. Unless the operator uses either the pastiles or the Kienboeck units for determining the amount of X-ray given the patient severe and fatal burns may result in a very short time."

Kenneth A. J. *Mackenzie.* (Portland). Personal Experiences with Radium in the Treatment of Cancer and Other Morbid Growths. Northwest Medicine, September, 1914, pp. 257-260.

"In 1910, while visiting the clinics in the city of Paris, I had occasion over a period of three months to observe in the Laboratoire Biologique du Radium the treatment of cancer and other growths by radium. I had heard and read a great deal of its therapeutic uses and regarded with doubt the efficacy of the emanations of radium in causing tumors of different kind to disappear."

"This attitude of doubt pursued me until I had the opportunities of observing the treatment of these diseases from day to day. One of the first cases was an epithelial cancer affecting the ala of the nose, which had been partially destroyed by the disease. At the same time I observed a rodent ulcer affecting the eyelid at the outer canthus, covering an area of two inches and threatening the destruction of the eye. I watched these two cases and noted after the first two or three days a perceptible improvement which continued slowly but steadily, so that at the end of ten weeks the growths had entirely disappeared, leaving little or no tract behind."

"I witnessed also several striking cases of angioma in little children affecting different parts of the head; one particularly occupied a position at the end of the nose, another the lobe of the ear, another on the hairy scalp, all of them prominently placed, elevated above the level of the skin and showing signs of rapid growth. The treatment of these cases was observed from day to

day until they disappeared without a stain on the skin left to tell that they had ever existed."

"Several cases of keloid were noted in scars, the result of burns, which possessed all the characters of new growths, especially those of proliferation and recurrence. Not one of these cases failed to respond to the curative action of radium."

"Some very striking results were observed in the treatment of the different forms of lupus, the so-called tuberculous type, and also lupus erythematosus. In several of the surgical clinics in Paris radium was used as a measure of prevention after large operations designed for the removal of cancer affecting the various organs. Professor *Delbet,* after removing a cancer of the breast which was very extensive and adherent with involvement of the glands in the axilla, placed a tube containing radium in that part of the wound which was most involved, the motive being to destroy, by the selective action of radium, any tissues or cells that might tend to cause reinfection or recurrence.

"In operations upon the uterus, where the cervix was the seat of cancer, following the resection that was necessary, radium of great activity was placed within the uterine canal to destroy any remnant of the disease and prevent its recurrence. In cancer of the hollow viscera, the stomach, the pylorus, the rectum, etc., following operations for the radical extirpation of the disease, tubes of radium were placed for the same purpose and retained for twenty-four hours or longer."

"In many cases, where recurrence had ensued after an operation, the initial nodules were treated by exposure to radium placed in proper apparatus for its direct application."

"The use of radium is not advocated in all cases of cancer by even its most enthusiastic exponents. The first thought always should be the earliest extirpation of the disease and upon this principle must rest the hope of its cure and its prevention. There are many instances, however, in early cancer in which radium possesses wonderful advantage over all other methods of treatment. It is rapid, radical and searching and, having a deeper penetration than even the knife, it reaches safely the concealed depths and the lurking places of the disease and eradicates it. It inflicts no shock; its operations are painless; no danger attends its use and it leaves no disfiguring marks."

"All forms of cancer which affect the surface of the body, no matter what their situation may be, offer the most attractive opportunities for treatment by radium. An epithelial cancer situated at the angle of the eye, the ala or bridge of the nose, or at an angle of the mouth, which are common situations, there being no metastatic deposit, yields promptly to radium without leaving any disfiguring scar behind. Under the same conditions the surgeon's knife would mutilate and disfigure."

"The minor uses of radium are very well illustrated in the treatment of the ordinary wart which disappears very quickly after a few exposures to the mixed rays. In the same manner many moles, small dermoid tumors and flat, pigmented vascular stains upon the skin are readily destroyed by exposure to a properly selected radium apparatus. Remarkable results are obtained

in the treatment of inveterate forms of circumscribed skin disease, such as ancient patches of psoriasis and eczema, and, when all other means have failed, radium has relieved the most intractable forms of pruritus."

"Radium will even reach, when adapted properly, malignant processes deeply situated in the body. I have recently treated a case of cancer of the lower jaw which was regarded as inoperable by the surgeon who referred the case and, regarding it as inoperable myself, I applied, without fear of the consequences, a small apparatus of radium at its full strength. After many days and weeks it finally yielded completely to treatment.

"A superficial epithelioma affecting the bridge of the nose, which came to my service from Idaho, and which had penetrated the bone, yielded after one hundred and fifty hours of exposure, at the rate of five hours per day. The results were not apparent, however, until three months afterwards, when the report came that the disease had vanished and that there was no scar left to tell the tale."

"Radium has wonderful influence in relieving local pains and I have known persistent neuralgias to be relieved by a few repeated applications. In two or three cases of intractable irritation of the bladder, attended with the formation of carbuncles, I witnessed complete relief of the symptoms with the disappearance of these growths."

"On tawny and coffee colored patches found upon the surface of the body, which are hairless and extensive in area, radium has no particular effect, whereas, on all hairy deeply colored tumors, commonly known as moles, the destructive or caustic action of radium is very effective, and, in the treatment of those hairy nevi, known as "beauty spots," which are prominent and thickly covered with hair, its levelling and depilatory action is of great value. It is well known that such growths not infrequently undergo malignant transformation and it is comforting to know that radium prevents this tendency."

"As I observed in the cases which were treated in the Laboratoire Biologique du Radium, in Paris, those which were amenable to treatment by radium were separated from those which were not and treated accordingly. I have known Dr. *Wickham* a great many times to tell men and women suffering from advanced cancer that radium could not possibly cure them. When radium was used in advanced cases it was used for the topical effect, just as other agencies are used for the relief of pain."

"Although the range of experience of the writer has been limited, he can point with great satisfaction to the treatment of a very considerable group of cases which, treated by radium, have shown very striking results, the best having been obtained in the treatment of malignant diseases, especially cancers. The complete list, however, includes also cases of sarcoma, rodent ulcer, angioma or nevi of different kinds, especially the prominent arteriovenous variety, pigmentary nevi, keloids and disfiguring scars, lupus, the tubercular form, and lupus erythematosus, inveterate and chronic patches of skin disease, urethral carbuncles, warts, moles and certain chronic neuralgias."

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